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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,013	03/21/2001	Gunther Braum	HUBR-1179 (10	1313

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EXAMINER	
LUKTON, DAVID	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/763,013	BRAUM ET AL.	
	Examiner	Art Unit	
	David Lukton	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Pursuant to the directives of the amendment filed 4/30/04, claims 1, 4 and 6 have been amended. Claims 1-6 remain pending. Applicants' arguments filed 4/30/04 have been considered and found persuasive in part. The §112, first paragraph rejection is withdrawn.

✧

Claims 1-6 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- In claim 1, the phrase "the completely synthesized peptide" lacks antecedent basis. In addition, if the peptide is indeed "completely synthesized", then what else is there to do? It is noted that the claim recites "closing the disulfide bridge", and implies that a disulfide bond is to be formed between two sulfhydryl groups on a peptide. The skilled artisan would infer from the specification that for a person endeavoring to prepare TT-232, the "completely synthesized" peptide would be TT-232 itself. But clearly, if additional process steps are required after already being in possession of the "completely synthesized" peptide, then what is the difference between the "completely synthesized" peptide that is not the final product of the synthesis, and the "completely synthesized" peptide that is the final product of the synthesis? The inconsistency would be quite apparent, even if it were not for the presence of claim 2. But claim 2 only adds to the confusion. Claim 2 mandates that, not only does one not have the target peptide prior to disulfide bond formation, but in addition, there are various protecting groups present which are clearly not part of the TT-232. Thus, what is meant by a "completely synthesized" peptide in the case of claim 2...? Does this refer to a molecule in which all of the requisite amino acids are present, and in the proper order, but that numerous additional process steps are required...? It is evident that the term "completely synthesized peptide" is not an accurate label.

- In claim 1, the phrase "the partially synthesized peptide" lacks antecedent basis at its first occurrence

- In claim 4, last line, the term "Bioatatin" is misspelled.

- In claim 4, the phrase "the completely synthesized peptide" lacks antecedent basis.
- In claim 4, the phrase "the partially synthesized peptide" lacks antecedent basis.
- In claim 6, the phrase "the completely synthesized peptide" lacks antecedent basis.
- In claim 6, the phrase "the partially synthesized peptide" lacks antecedent basis.

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1, 2, 4, 6 are rejected under 35 U.S.C. (103 as being unpatentable over Keri (EP 505,680) in view of Mutter, Manfred (Gross, Ed., "The Peptides", pages 291-329, Volume 2, Academic Press, New York, 1980).

As indicated previously, Keri discloses (e.g., page 20) synthesis of TT-232 on solid phase. Keri does not disclose preparation of TT-232 in solution. Mutter discloses methods of

peptide synthesis in which a polymeric group is bonded to the C-terminus of a growing peptide. The polymer, and the peptide bonded thereto, are soluble in the solvent that is being used, thereby meeting the requirements of the claims. Mutter also discloses that this method has advantages over solid phase synthesis methods. Advantages are described, e.g., at the following locations: page 291, last paragraph; page 297, last paragraph, and page 301, line 4+. Mutter does not describe a synthesis of TT-232.

In response to the foregoing, applicants have restated the examiner's observations with regard to what the references do teach, and do not teach. Applicants conclude, without reasoning, that Mutter and Keri together do not teach synthesis of TT-232 in solution *per se*. It is not clear what applicants intend by solution *per se*. The Mutter process calls for synthesis of peptides in "solution". A compound is in "solution" if it is soluble. Applicants have presented no evidence that a chemist synthesizing TT-232 according to the Mutter procedure would not produce a series of synthetic intermediates in solution. Applicants have also argued that the instant claims exclude peptide synthesis in solution, if solubility is dependent on the presence of a polymer. However, there is no such exclusion. The claims require only that one couple (partially) protected amino acids in sequence, such that the synthetic intermediates thereby obtained are soluble in solution. A practitioner of the Mutter procedure would be doing just that. It is true that the claims are silent as to the presence of a polymeric group. However, there is nothing in the language of the claims to exclude it either.

The rejection is maintained.

✧

Claims 1, 2, 4, 6 are rejected under 35 U.S.C. §103 as being unpatentable over Keri (EP 505,680) in view of Bernard (USP 5,712,367).

As indicated previously, Keri discloses (e.g., page 20) synthesis of TT-232 on solid phase. Keri does not disclose preparation of TT-232 in solution. Bernard discloses a method of peptide synthesis in which the peptide is solubilized by means of a lipophilic group bonded to the C-terminus. Also disclosed (e.g., col 2, line 17+) are disadvantages of solid phase peptide synthesis, and (col 8, line 6+) advantages of the disclosed method. Bernard does not describe a synthesis of TT-232.

Applicants have made the same arguments in their traversal of this rejection as were made in the traversal of the rejection over Keri in view of Mutter. Applicants have also argued that the instant claims exclude the presence of a lipophilic group at the C-terminus of the growing peptide. However, there is in fact no such exclusion.

The rejection is maintained.

✧

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached at 571-272-0925. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

DAVID LUKTON
PATENT EXAMINER
GROUP 1600